

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/BE 03/00192

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/28 C07K16/46 A61K39/395 C12N15/13  
G01N33/577 A61P37/06 A61P19/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, WPI Data, PAJ, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 91/02078 A (PEPTIDE TECHNOLOGY LTD) 21 February 1991 (1991-02-21) page 3, line 28 -page 4, line 24 page 15, line 25 - line 33	1
Y	---	2-49
Y	ELS CONRATH K ET AL: "Camel single-domain antibodies as modular building units in bispecific and bivalent antibody constructs" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 276, no. 10, 9 March 2001 (2001-03-09), pages 7346-7350, XP002248402 ISSN: 0021-9258 the whole document	2-49
	---	
	---/---	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

\* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

7 May 2004

14/05/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Le Flao, K

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/BE 03/00192

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>VALLE E ET AL: "Infliximab"  EXPERT OPINION ON PHARMACOTHERAPY, ASHLEY,  LONDON,, GB,  vol. 2, June 2001 (2001-06), pages  1015-1025, XP002965315  ISSN: 1465-6566  the whole document</p> <p>---</p>	1-49
Y	<p>WO 02/057445 A (MURUGANANDAM ARUMUGAM  ;STANIMIROVIC DANICA (CA); NARANG SARAM  (CA)) 25 July 2002 (2002-07-25)  page 18, line 29 -page 47, line 18</p> <p>---</p>	1-49
A	<p>WO 02/079781 A (ANDREWS JANET S ;HESKA  CORP (US); JENSEN WAYNE A (US); MCDONALD  TH) 10 October 2002 (2002-10-10)  page 26, line 25 -page 28, line 21  page 29, line 14 - line 20</p> <p>---</p>	4
A	<p>TANHA J ET AL: "Selection by phage  display of llama conventional VH fragments  with heavy chain antibody VHH properties"  JOURNAL OF IMMUNOLOGICAL METHODS,  ELSEVIER, AMSTERDAM, NL,  vol. 263, no. 1-2,  1 May 2002 (2002-05-01), pages 97-109,  XP004354388  ISSN: 0022-1759  the whole document</p> <p>---</p>	1-49
A	<p>D'HAENS G ET AL: "ENDOSCOPIC AND  HISTOLOGICAL HEALING WITH INFlixIMAB  ANTI-TUMOR NECROSIS FACTOR ANTIBODIES IN  CROHN'S DISEASE: A EUROPEAN MULTICENTER  TRIAL"  GASTROENTEROLOGY, SAUNDERS, PHILADELPHIA,  PA., US,  vol. 116, no. 5, May 1999 (1999-05), pages  1029-1034, XP009009036  ISSN: 0016-5085  the whole document</p> <p>-----</p>	1-47

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/BE 03/00192

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☒ Claims Nos.: 22-24  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Continuation of Box I.2

Claims Nos.: 22-24

Present claims 22-24 relate to a product defined by reference to a desirable characteristic or property, namely "an unknown agent that modulates the binding of an anti-TNF-alpha polypeptide of any of claims 1 to 11, and 13 to 16 to Tumor Necrosis Factor-alpha" (claim 22) and "an unknown agent that modulates Tumor Necrosis Factor-alpha-mediated disorders" (claim 23). The scope of claims 22-24 is unclear and speculative within the meaning of Article 6 PCT. Said claims lack indication concerning their technical features. The available experimental data actually relate to anti-TNF-alpha single domain antibodies and their preparation, but not to an agent that modulates their binding. Consequently no search has been carried out for the claims 22-24.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/BE 03/00192

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9102078	A	21-02-1991	AU 640400 B2	26-08-1993
			AU 6145490 A	11-03-1991
			WO 9102078 A1	21-02-1991
			EP 0486526 A1	27-05-1992
			CA 2064915 A1	08-02-1991
			DE 69027121 D1	27-06-1996
			DE 69027121 T2	14-11-1996
			DK 486526 T3	24-06-1996
			JP 3443119 B2	02-09-2003
			JP 2003096096 A	03-04-2003
			JP 2003231699 A	19-08-2003
			US 2003162948 A1	28-08-2003
			US 2003232970 A1	18-12-2003
			US 2004002588 A1	01-01-2004
			US 2003171553 A1	11-09-2003
			US 2003166874 A1	04-09-2003
			US 2003216552 A1	20-11-2003
			US 2004002589 A1	01-01-2004
			US 2003208047 A1	06-11-2003
			US 5644034 A	01-07-1997
			US 2003171554 A1	11-09-2003
			US 2003171555 A1	11-09-2003
			US 2004002590 A1	01-01-2004
			US 2003225254 A1	04-12-2003
			US 6416757 B1	09-07-2002
			US 2003232971 A1	18-12-2003
			US 6593458 B1	15-07-2003
			US 2001018507 A1	30-08-2001
			US 2001023287 A1	20-09-2001
			US 2001018508 A1	30-08-2001
WO 02057445	A	25-07-2002	AU 6885501 A	03-12-2001
			WO 0190190 A2	29-11-2001
			WO 02057445 A1	25-07-2002
			CA 2380443 A1	29-11-2001
			CA 2441903 A1	25-07-2002
			EP 1328626 A1	23-07-2003
			US 2003190598 A1	09-10-2003
WO 02079781	A	10-10-2002	CA 2442074 A1	10-10-2002
			EP 1384075 A1	28-01-2004
			WO 02079781 A1	10-10-2002
			US 2003022262 A1	30-01-2003